Elevated Symptom Prevalence Associated with Ventilation Type in Office Buildings

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The California Healthy Building Study was designed to assess relations between ventilation system type and office worker symptoms in a set of U.S. buildings selected without regard to worker complaints. Twelve public office buildings in northern California meeting specific eligibility criteria were studied in the summer of 1990: three naturally ventilated, three mechanically ventilated (without air conditioning), and six air-conditioned buildings. Questionnaire data were collected from 880 workers in selected spaces within the study buildings. We adjusted effect estimates for various ventilation types for personal, job, and work place factors using logistic regression, and alternatively, using a mixed effects model (SAS/GLIMMIX) to adjust for correlated responses within study spaces. Higher adjusted prevalences of most symptom outcomes were associated with both mechanical and air-conditioned ventilation, relative to natural. With a conservative adjustment for problem building status, the highest adjusted prevalence odds ratios from logistic regression models were for dry or itchy skin [mechanical: odds ratio (OR) = 6.0, 95% confidence interval (CI) = 1.6–22; air-conditioned: OR = 6.0, 95% CI = 1.7–21] and lower respiratory symptoms (mechanical: OR = 2.9, 95% CI = 0.7–11; air-conditioned: OR = 4.0, 95% CI = 1.1–15). GLIMMIX estimates were similar, with slightly wider confidence intervals. Reporting bias was small. These findings of symptom increases within mechanically ventilated and air-conditioned U.S. buildings support previous findings available only from European buildings. (Epidemiology 1996;7:583–589)

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Outbreaks of building-related illness in offices, involving recognized infectious disease, hypersensitivity disease, or toxicity from known pollutants, have been well documented.[1] More common, however, are apparent outbreaks of illness within office buildings in which neither environmental causes nor recognized diseases can be identified. Mostly reported within the last 20 years, these episodes are often called sick building syndrome (SBS).[2] Sick building syndrome is characterized by widespread complaints of nonspecific symptoms (for example, mucous membrane irritation, upper respiratory problems, skin irritation, headache, and fatigue), but no clinical sign or laboratory abnormality.[1]

Various European epidemiologic studies have examined office worker symptoms within multiple office buildings of different ventilation types, chosen without regard to worker complaints.[3-12] In these studies, higher symptom prevalences were generally not related to measured contaminant concentrations. Almost without exception, however, these studies found symptom prevalences to be higher within air-conditioned buildings, even without humidification, than within naturally ventilated buildings.[4-12,13] Findings for mechanical ventilation systems *without* air conditioning have been inconsistent.[1,11,12,14,15] None of these studies assessed the role of reporting bias due to occupant concerns about air-conditioned buildings.

The relation of worker symptoms to building ventilation type has not been studied previously within the United States. To address this question, the California Healthy Building Study investigated the association of work-related symptoms with mechanical ventilation and with air conditioning, relative to natural ventilation,

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after adjustment for potential confounding by personal, job, and work space factors, and with assessments of potential reporting bias. Additional information on study design and methods, and additional study objectives, have been reported previously.[16,17]

Subjects and Methods

Study Design and Population

We studied workers in public office buildings in the San Francisco Bay Area of California between June and September 1990. Buildings were selected, without regard to previous worker complaints, from city- and county-owned office buildings meeting specific eligibility criteria[17] and having one of three types of ventilation: natural ventilation (ventilation only by operable windows); mechanical ventilation (mechanical supply and exhaust ventilation with *no* air conditioning and *no* humidification, and with operable windows); and air conditioning (mechanical supply and exhaust ventilation *with* air conditioning and *no* humidification, and with *sealed* windows).

Among eligible buildings, refusals came from 1 of 4 naturally ventilated buildings (no reason provided), 1 of 4 mechanically ventilated buildings (no reason provided), and 5 of 11 air-conditioned buildings (4 refusals due to serious worker/management tensions about occupant health issues, 1 refusal due to insufficient occupant time). We included all 12 buildings that granted permission. Smoking within all of these buildings was prohibited except, within some buildings, in small designated areas not linked by ventilation to the rest of the building. The average daily maximum summer temperatures in the three included counties varies from 69°F in San Francisco to 86°F in Contra Costa County, with essentially no summer rain and moderate (<60%) humidity.

To study a representative set of buildings, we neither sought nor excluded "problem buildings"[18] with widespread occupant concerns about indoor air quality and health. Because symptom reports from such buildings may be upwardly biased by occupant concerns, our analysis included adjustment for problem building status. Only one of our study buildings (#2), an air-conditioned building, was found to be a classic problem building, with a history of persistent occupant health complaints and unsuccessful health investigations. In our target population, however, four of the five air-conditioned buildings not made available for study were potentially problem buildings as well.

Within each building, we studied only workers from specific study spaces. We selected the largest open office areas available, containing together at least 45 workers, along with adjoining enclosed offices. Overall, we included 29 study spaces from the 12 buildings, with the number of workers per space ranging from 3 to 77. All of these workers were eligible if they had worked in the building at least 3 months, worked there at least 20 hours per week, and were not absent from the office for a week or more during the study period.

We obtained building information from records, physical inspections, and interviews with building management and engineering staff, and we made a variety of environmental measurements.[17] All environmental contaminants measured were below any existing occupational health standards or guidelines, and the measured indoor environmental parameters, by the metrics used in preliminary analyses, showed little relation to symptoms.

Questionnaire

The questionnaire was a modified version[16] of a self-administered questionnaire used in several U.S. government building studies.[19,20] Data reported here came from two questions asked about 15 symptoms: "How often during the LAST YEAR did you experience this symptom while working in the building?" (responses: never, rarely, sometimes, often, always) and "Does the symptom usually change when not at work? (responses: gets worse, stays the same, gets better). Other questions assessed health, demographic, psychosocial, and job-related parameters.

Analytical Methods

Outcome Variables

We defined a "work-related symptom" as one that occurred often or always at work in the previous year and also improved away from work. We analyzed eight outcomes (Table 1), using data on 12 specific symptoms. We constructed seven of these outcomes from individual symptoms previously reported to be related to indoor air factors and ventilation type[1]: two outcomes came directly from individual symptom questions (eye symptoms, skin symptoms), and five outcomes were symptom groupings based on common organ systems, hypothesized mechanisms, or previous reports. We defined three of the symptom group outcomes to require at least one work-related symptom within that group (nose or throat, lower respiratory, headache or fatigue). As indices of relatively more severe symptom outcomes, two multiple symptom group outcomes required multiple work-related symptoms within the symptom group (multiple lower respiratory, requiring both of the two relevant symptoms; multiple mucous membrane, requiring three of the four relevant symptoms). For the multiple lower respiratory symptom outcome, regression models would not converge, owing to zero prevalence in the naturally ventilated buildings. For this outcome, we expanded the definition of a work-related symptom to include symptoms experienced sometimes, often, or always during the previous year, and improving away from work. (Prevalences by the original and expanded definitions can be compared in Table 2.)

The eighth outcome analyzed, the "non-indoor air-related" symptom group, required at least one work-related symptom of three symptoms not previously reported to be associated with indoor air factors or ventilation type: toothache, earache, and pain in neck or shoulder. We assumed that actual prevalence of these symptoms, although possibly related to various physical or psychological work stressors, or some indoor climatic

TABLE 1. Symptom Outcomes* Used in Analysis

Eye symptoms	
	Dry, irritated, or itching eyes
Skin symptoms	
	Dry or itchy skin
Nose or throat symptoms (at least 1 of)	
	Runny nose
	Stuffy nose/sinus congestion
	Dry or irritated throat
Lower respiratory symptoms (at least 1 of)	
	Chest tightness
	Difficulty breathing
Headache or fatigue (at least 1 of)	
	Headache
	Unusual fatigue or tiredness
Multiple lower respiratory symptoms (both of)	
	Chest tightness
	Difficulty breathing
Multiple mucous membrane symptoms (at least 3 of)	
	Dry, irritated, or itching eyes
	Runny nose
	Stuffy nose/sinus congestion
	Dry or irritated throat
Non-indoor air-related symptoms (at least 1 of)	
	Earache
	Toothache
	Pain or numbness in shoulder/neck

* A work-related symptom, unless otherwise specified, was defined as one that occurred often or always when at work during the previous year and that also improved when away from work.

conditions, should not differ by ventilation type. Increased reporting of these symptoms would thus suggest symptom overreporting.

Independent Variables

Models included indicator variables for the ventilation type categories, mechanical ventilation and air conditioning, relative to natural ventilation. We used a covariate term for "problem building status" to adjust for any unusual psychosocial influences on symptom reporting in the one problem building. We used other covariate terms, shown in Table 3, to adjust for potential confounding by personal, job, and work space characteristics.

Analyses

For analyses, we used SAS version 6.08, PROC LOGISTIC,[21] and GLIMMIX,[22,23] a SAS Macro. We calculated crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for associations between each of the eight symptom outcomes and ventilation type.[24] We estimated adjusted ORs in both logistic regression and mixed effects logistic regression (GLIMMIX) models.

Logistic Regression Models

For each outcome, we included in the initial full multivariate model all covariates for which the *P*-value in a bivariate model was less than 0.25. Potential covariates are listed in Table 3. We included terms for the two ventilation types and problem building status in all models. We reduced the initial models by removing covariates for which the *P*-value was less than 0.20, except

TABLE 2. Crude Prevalence of Work-Related Symptoms* in the Study Population of Workers

	Ventilation Type and Building Numbers															
	Natural Ventilation				Mechanical Ventilation				Air Conditioning							All Buildings (1–12)
Symptoms	1	10	12	All	6	9	11	All	2†	3	4	5	7	8	All	
Eye symptoms	15.0	9.4	14.8	13.5	15.0	10.2	29.5	20.4	37.7	17.0	23.2	14.3	20.4	20.5	24.3	22.0
Skin symptoms	2.6	3.2	1.9	2.4	7.3	2.0	15.4	9.5	22.4	9.0	11.1	2.0	19.1	3.8	13.1	10.8
Nose or throat symptoms	24.4	28.1	12.7	20.3	39.0	24.0	29.5	30.2	56.8	29.7	43.2	16.0	33.7	22.9	37.7	33.7
Lower respiratory symptoms	0.0	6.2	1.8	2.4	7.3	0.0	10.8	6.8	16.6	3.4	10.0	4.0	6.7	4.9	8.8	7.5
Headache or fatigue	26.3	24.2	23.6	24.6	36.6	12.8	37.0	29.8	57.1	28.6	44.0	34.0	31.8	19.5	38.6	34.9
Multiple mucous membrane symptoms	7.3	0.0	3.6	3.9	9.8	4.0	14.1	10.1	21.0	12.1	15.3	4.0	10.1	10.8	13.8	11.6
Multiple lower respiratory symptoms	0.0	0.0	0.0	0.0	4.9	0.0	1.4	1.9	6.9	0.0	5.4	0.0	2.3	1.2	3.4	2.6
Multiple lower respiratory symptoms‡	5.6	3.2	7.6	5.8	12.2	2.3	18.3	12.2	18.4	5.7	9.3	2.0	10.5	4.9	9.9	9.7
Non-indoor air-related symptoms	15.0	15.2	14.6	14.8	14.6	12.2	14.3	13.8	20.0	15.4	16.4	16.0	13.5	10.8	15.8	15.3
Number	41	34	55	130	41	50	79	170	151	96	111	50	89	83	580	880

* Often or always in the last year, unless otherwise specified.
† Building with "problem" history.
‡ Sometimes, often, or always in the last year.

TABLE 3. Covariates* Used in Regression Models

Building factors
Ventilation type
Problem building status
Personal factors
Gender
Age
Race
Education
Smoking
Asthma
Pollen allergy
Psychosocial factors
Job stress
Job dissatisfaction
Job factors
Job type
Time per day using photocopiers
Time per day using computers
Months in building
Hours per week in building
Work space factors
Sharing work space with other workers
Cloth partitions
Carpets
Distance from a window
Ability to see out a window
Amount of natural light

* Ventilation type, race, and job type covariates were multicategorical; all others were dichotomous.

when their removal changed ventilation type estimates by more than 10%.

Initially, we included the covariate term for problem building status in all models. To explore the influence of this building on the effect estimates, we created two alternate sets of logistic regression models, one excluding the covariate term for problem building status, and one excluding all data from the problem building.

Mixed Effects Models

Because respondents were selected in clusters by study spaces, the sample may have had less variability than if individuals had been selected independently. Conventional logistic models assume independent individual observations and may exaggerate the precision of estimates in such cases. We used GLIMMIX with an "exchangeable correlation structure" to adjust for the possible non-independence of individuals within study spaces.

Results

The response rate among eligible workers was 85% overall and similar among the three ventilation types, with 880 completed questionnaires received. Detailed information about study participants has been reported previously.[17] Seventy-two per cent of the workers were women; 65% were over 39 years old; 46% were white; 44% were clerical, and 48% were professionals or managers; 47% had less education than a bachelor's degree; and 18% were current smokers.

Table 2 shows the crude prevalence of work-related symptom outcomes for each building, each ventilation type, and the total study population. Prevalences are shown for multiple lower respiratory symptoms using both the regular and modified definitions. Among the symptom outcomes, overall prevalences were highest for headache or fatigue (34.9%) and nose or throat symptoms (33.7%) and lowest for multiple lower respiratory symptoms (2.6%). Symptom prevalences showed substantial variation within ventilation types but were generally lower within naturally ventilated buildings, with the highest prevalences for all symptom outcomes in an air-conditioned building (#2).

Crude ORs (not shown) were somewhat elevated for both mechanically ventilated and air-conditioned buildings, relative to naturally ventilated buildings, for all symptoms hypothesized to be related to indoor air. These ORs, except for multiple lower respiratory symptoms, were highest in the air-conditioned buildings. No elevation was seen for non-indoor air-related symptoms.

Table 4 shows adjusted ORs from the logistic regression models, both with and without the problem building status covariate. Adjusted ORs for both ventilation types were elevated for all symptoms hypothesized to be related to indoor air. Non-indoor air-related symptoms showed little or no increase for either ventilation type. The highest adjusted ORs in both ventilation types were for skin symptoms, lower respiratory symptoms, and multiple mucous membrane symptoms.

Table 4 also shows that inclusion of a problem building term in the model had little effect on symptom estimates for mechanically ventilated buildings, but it consistently lowered estimates for air-conditioned buildings. Adjusting for problem building status lowered all symptom ORs even more than excluding problem building data entirely (not shown).

OR estimates from GLIMMIX models, shown in Table 4, were generally similar to, and within about 10% of, estimates from logistic models. Confidence intervals from GLIMMIX models were also similar to those from logistic models. Most were slightly wider, by about 10%, but they were somewhat narrower for the two least common outcomes.

Discussion

Choice of Analytic Approach

The goal of these analyses was to produce minimally confounded estimates of effect of two ventilation types on office worker symptoms in a set of office buildings representative, to the extent feasible, of three ventilation types.

Our adjustment for problem building status assumes that the problem building contained unique psychosocial influences, requiring separation in the analysis from the effects of environmental exposures, *in addition to* adjustment for job stress and job satisfaction. Prevalence of the "non-indoor air-related" symptoms in the problem building was, in fact, approximately 30% higher than in the other air-conditioned buildings, indicating some overreporting. Still, this 30% elevation cannot explain the approximate 100–400% excess of other symptoms in the problem building relative to the rest of the air-

TABLE 4. Adjusted* Odds Ratios (ORs) and 95% Confidence Intervals (CI) for Work-Related Symptoms† by Ventilation Type, Relative to Naturally Ventilated Buildings, Using Logistic Regression and GLIMMIX Models

	OR (95% CI) by Ventilation Type					
	Mechanical Ventilation			Air Conditioning		
	Logistic Regression			Logistic Regression		
Work-Related Symptoms	Without Problem Building Term	With Problem Building Term	GLIMMIX With Problem Building Term	Without Problem Building Term	With Problem Building Term	GLIMMIX With Problem Building Term
Eye symptoms	1.8 (0.9–3.5)	1.7 (0.9–3.4)	1.7 (0.8–3.6)	2.5 (1.4–4.5)	2.1 (1.1–4.0)	2.1 (1.1–4.2)
Skin symptoms	6.2 (1.7–23)	6.0 (1.6–22)	5.8 (1.4–24)	6.7 (2.0–22)	6.0 (1.7–21)	6.1 (1.6–23)
Nose or throat symptoms	1.8 (1.0–3.3)	1.8 (1.0–3.2)	1.6 (0.8–3.2)	2.5 (1.5–4.2)	1.9 (1.1–3.2)	1.7 (0.9–3.2)
Lower respiratory symptoms	2.8 (0.7–11)	2.9 (0.7–11)	3.2 (0.9–11)	5.6 (1.6–19)	4.0 (1.1–15)	4.1 (1.2–14)
Headache or fatigue	1.2 (0.7–2.3)	1.3 (0.7–2.4)	1.3 (0.7–2.4)	2.0 (1.2–3.3)	1.5 (0.9–2.5)	1.5 (0.8–2.6)
Multiple mucous membrane symptoms	3.4 (1.2–9.7)	3.3 (1.2–9.5)	3.1 (0.9–10)	4.3 (1.7–11)	3.4 (1.3–9.1)	3.5 (1.2–10)
Multiple lower respiratory symptoms‡	3.0 (1.1–8.2)	2.9 (1.0–8.0)	2.7 (1.1–7.0)	3.5 (1.4–8.9)	2.8 (1.1–7.6)	2.7 (1.1–6.7)
Non-indoor air-related symptoms	1.0 (0.5–2.1)	1.0 (0.5–2.1)	1.0 (0.5–2.2)	1.1 (0.6–2.0)	1.1 (0.6–2.0)	1.1 (0.6–2.1)

* See Table 3 for independent variables potentially included in model.
† Often or always in the last year, unless otherwise specified.
‡ Sometimes, often, or always in the last year.

conditioned buildings. Thus, adjusting models for problem building status, which essentially allocates to overreporting all of the excess risk in that building over other air-conditioned buildings (and lowers all OR estimates for air-conditioned buildings more than omitting the problem building data entirely), is likely to be overly conservative. Nevertheless, this decision affects only whether air-conditioned buildings are associated with *additional* excess risk over mechanical ventilation.

Mixed effects models, although in principle more appropriate than conventional logistic models for observations selected in clusters, have not been used previously in office building studies. Mixed effects models should, in theory, produce the same point estimates but with wider confidence intervals. GLIMMIX, relative to logistic models, did produce similar ORs and, except for the two least common outcomes, slightly wider confidence intervals. Interpretation of the findings is thus little affected by use of mixed effect models.

As GLIMMIX assumes large numbers of clusters, the 29 clusters in our data may have been too few. Logistic regression may thus be acceptable for other data with similar departures from independence. For datasets containing more clusters, mixed effect models may be preferable.

Interpretation of Findings

Regardless of the analysis methods used, we found higher prevalences of a number of work-related symptoms among workers in California office buildings with mechanical supply and exhaust ventilation, with or without air conditioning. Without the presumably overly conservative adjustment for problem building status, symptoms within air-conditioned buildings were uniformly higher than in mechanically ventilated buildings. Overall symptom patterns did not point to specific mechanisms.

Comparable data, using representative sets of buildings, similarly specific ventilation categories, and estimates adjusted for multivariate confounders (but not for problem buildings) are available from two other studies, both European.[11,12] These studies both showed modest elevations of symptoms, with ORs generally below 1.5 in mechanically ventilated buildings and slightly higher elevations, with ORs less than 2.0, in air-conditioned buildings. These studies agree with ours for eye symptoms and (reported previously) for headache and fatigue.[17] ORs for skin symptoms were substantially higher in the California study. Other studies have not assessed the lower respiratory, multiple lower respiratory, or multiple mucous membrane symptom outcomes, for which ORs in this study were around 3 or higher.

The overall prevalences of some work-related symptoms in our study population were high: 35% for headache or fatigue, and 34% for nose or throat symptoms. Symptom prevalences in other cross-sectional office worker surveys have been similarly high,[4] including surveys from the United States and Canada.[25–27] These estimates depend heavily on the definitions used but nevertheless indicate a potentially widespread problem.

Limits to Interpretation

Because the study included only workers from 12 public office buildings in a limited geographical area and during one season, the results may not be representative of other U.S. office buildings, in different climates or during other seasons. A number of potential biases still may have influenced these findings. Careful enumeration of all eligible buildings reduced bias in building selection, but the high building refusal rate among air-conditioned buildings, owing to worker environmental dissatisfaction, likely caused underestimates of symptom prevalence within the air-conditioned buildings in our target population. Selection bias at the worker level may also have resulted in underestimation of actual associations, if workers with building-related health problems had left jobs in their buildings or were absent because of illness more often than others.

Substantial individual response bias is unlikely, because response rates were high and similar within all ventilation types. As respondents were not aware of study hypotheses, and questionnaires were self-administered, this potential source of response bias cannot explain the associations found.

Current studies of sick building syndrome, lacking objective health measures, are susceptible to bias from worker concern about health effects of indoor air quality. In this study, we assessed such overreporting in two ways. First, symptom increases in our study were as high within the older mechanically ventilated buildings with operable windows as within most of the newer sealed air-conditioned buildings. Thus, worker concerns based on media reports about specific symptoms in predominantly new, air-conditioned buildings were not a likely explanation for our findings. Second, the OR for non-indoor air-related symptoms was only slightly elevated in mechanical or air-conditioned buildings, much less than were most other symptoms in these groups. In the problem building, non-indoor air-related symptoms were much less elevated than other symptoms. This finding indicates that overreporting in the study was modest, even in the single building where it was most likely.

Possible Explanations for Findings

Some factor(s) associated with mechanical or air-conditioned ventilation systems in these buildings may be causing increased symptoms. Humidification systems, posing known microbiological exposure risks, were not present in any of the study buildings. The absence, or concerns about absence, of operable windows cannot explain the elevated risks found, because the mechanically ventilated buildings had operable windows. The most likely explanation for our findings is an association of both ventilation type and symptom prevalence with at least one of the following: physical features related to building age; inadequate thermal conditions or outside air supply; or the production or dissemination of contaminants by ventilation systems.

The mean age for naturally ventilated buildings was 65 years, for mechanically ventilated, 49 years, and for air-conditioned, 18 years. Newer buildings did not show the simple association with symptoms reported elsewhere,[9,28] as even older mechanically ventilated buildings had elevated symptom prevalence. Nor was a relation apparent between building age and symptoms *within* ventilation types. Thus, it seems unlikely that factors related to building age but not assessed in this study, even if related to symptoms, could have caused substantial confounding without strong age/symptom associations.

In this study, the measure of predicted thermal discomfort used in preliminary analyses did not contribute to prediction of symptom outcomes.[17] Some studies have found temperature in offices to be related to prevalence of work-related symptoms,[15,25,29–31] although associations between ventilation type and thermal discomfort have not been reported,[6,32,33] except in one study.[34]

Supply of less outside air might elicit symptoms by causing higher concentrations of indoor-produced pollutants. Overall evidence from other studies indicates symptom increases with lower outside air ventilation rates.[3,14,26,30] Preliminary analyses of these data showed no important association between mean indoor carbon dioxide concentrations and symptom outcomes, although the low CO_2 levels in our study buildings provided limited ability to assess such relations.[17] Only in one building (#4) did we find a weekly mean concentration even as high as 580 ppm. Volatile organic compounds (VOCs) specifically can be affected by ventilation rate, but, in preliminary analyses, we did not find total VOC concentrations to be materially related to symptom outcomes.[17] (In other analyses, we have found relations between specific irritant symptoms and more complex metrics of VOCs; for example, VOC clusters from water-based paints or solvents.[35,36])

One credible hypothesis for the associations reported here has been proposed previously: that mechanical ventilation and air conditioning systems may disseminate contaminants that cause occupant symptoms but are not characterized by conventional exposure assessments.[4,6,37–40] Previous research has indicated that building ventilation systems may themselves be *sources* of perceived pollutants[41] or indoor air contaminants, such as microorganisms[1,39,42,43] or VOCs.[44] A recent study has found the first association between ventilation systems and an increase in a measured indoor air contaminant: endotoxin from Gram-negative bacteria.[39]

Most earlier studies have not found associations in office buildings between increased symptom prevalence and specific measured airborne contaminants.[1,15,32,45] Some recent field[15,27,39,46–51] and chamber[52–57] studies have found such relations. Although these findings require confirmation, they indicate, along with indirect findings such as those from this study, potential environmental etiologies for office worker symptoms.[3] Identification of specific causes may require new indoor environmental measurement techniques.

Meanwhile, findings of multiple studies indicate that naturally ventilated buildings overall have lower levels of (unidentified) risk factors for symptoms and thus may provide relatively healthy "background" symptom ranges as goals for other building types.

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